Ultrasound synthesis, Spectral characterization and Biological evaluation of transition metal complexes of some novel β-diketones

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Abstract of proposed work plan :

In this research work β-diketones and its transition metal complexes will be synthesized by conventional as well as ultrasonic method. The synthesized compounds will be characterized for FTIR, ^{1}H-NMR, ^{13}C-NMR, UV/VIS(DMSO), EC-MS. Also the antibacterial and antifungal activity will be carry out for these compounds.

1] Introduction:

One of the charming features of modern coordination chemistry is the ever growing academic, commercial and biological interest exhibited by metal complexes of organic molecules, both natural and synthetic. This is mainly due to the realization of vital role of metal complexes in biology and medicine, where much progress has been made during the last few decades. Thus numerous highly efficient synthetic metal complexes which mimic the behavior of complex biomolecules are known and at present the study of such compounds are receiving much attention.

The Pharmacological significance of metal complexes are dependent both on the nature of the metal ion and the type of the ligands coordinated. Thousands of new ligand systems have been developed in recent years because of the developments in modern synthetic organic chemistry. The peculiar chemical properties of metal-ligand complex also impart innovative pharmacological profiles to this class of therapeutic and diagnostic agents, most likely in relation to novel molecular mechanisms still poorly understood. This trend is evident from the reports on numerous compounds based on 1,3-diketones and related compounds. With the advancement in the field of inorganic chemistry the role of transition metal complexes as therapeutic compounds is becoming increasingly important.

As β-diketones are having such varied applications in pharmacology, we decided to synthesize a novel β-diketone and its transition metal complexes by ultrasound irradiation method. Ultrasound irradiation assisted organic synthesis is an efficient and eco-friendly synthetic strategy. Many homogeneous and heterogeneous reactions can be conducted smoothly by sonication to provide improved yields and increased selectivities.

β-diketone and its metal complexes have been widely used in diverse areas because of their unique structural features, chemical functionalities and electroluminescent materials due to enhanced stability in heat and light. β-diketones have gained a lot of interest due to their high reactivity with to form chelates, as

intermediate in the synthesis of core heterocycles such as flavones, pyrazole and keto-enol tautomerism. They show pharmacological activities like prophylactic antitumor, antibacterial and antioxidant and recently it is reported that they have the important pharmacophores for the HIV-integrase(1N) inhibitors.

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2] Review of Literature and Development in the subject (previous work done in the relevant area):

The importance of 1,3-diketones in synthetic organic chemistry is difficult to overestimate. Their accessibility, stability, and often unique properties make them promising for use in various fields of human activity. High reactivity of 1,3-diketones opens wide prospects for the design of a variety of organic compounds, including those structurally related to natural ones. Continuously growing interest in β-dicarbonyl compounds is observed among researchers working in various fields of medicinal chemistry and chemistry of metal complexes. Sol–gel syntheses with β-diketones afforded organic–inorganic hybrid materials used in gas sensors and molecular thermometers, as well as in the manufacture of optical fiber and light converting materials [1–5].

Over the past 10–15 years, not only selectivity parameters and overall yield of reaction products but also such factors as enhanced requirements to starting materials, reaction time, energy consumption, toxicity, etc., have acquired increasing significance in the assessment of the efficiency of chemical syntheses.

1,3-Diketones turned out to be excellent versatile intermediates in multicomponent reactions, in particular regio- and stereoselective, which is especially important in the synthesis of potentially biologically active compounds [6–9] .

β-diketone and its metal complexes have been widely used in diverse areas because of their unique structural features, chemical functionalities, and electroluminescence materials[10] due to enhanced stability in heat and light. . β-diketones have gained a lot of interest due to their high reactivity to form chelates[11] as intermediate in the synthesis of core heterocycles such as flavones[12], pyrazole[13] and keto-enol tautomerism. . β-diketones have shown pharmacological activities like prophylactic antitumor [14], antibacterial[15] and antioxidant[16] and recently it is reported that they have the important pharmacophores for the HIV-integrase(1N) inhibitors[17-18].

β-diketonato transition metal complexes have been the subject of many different investigations ranging from synthetic, kinetic and structural topics, to catalysis and electronic transfer processes. Vettaikaranpudur[19] investigated catalytic activity of mixed ligand complexes of Fe (III), Co (II), Ni (II), Cu (II) containing β-diketones and triphenyl phosphine. Mbabazi[20] studied further biologically active derivatives of 1,3-diketones by coupling aromatic aldehydes with 5,5-dimethylcyclohexane-1,3-dione(dimedone). Some of the Cu (II), Ni (II), Co (II) and VO (IV) complexes of β

diketones or 1-(3-hydroxy-2-napthyl)-5-(p-x-phenyl)pent-4-ene-1,3-diones were reported and characterized by elemental analysis, IR, electronic, 1H NMR, and ESR spectroscopic and by magnetic susceptibility measurements. It was reported that metal ions coordinated through both carbonyl oxygen atoms and the effect of conjugation of the ligand structure ($d\pi$-π^* interaction) was strong enough to stabilize the metal ligand bond[21]. Voloshin[22] studied monothio-β-diketone ligands suitable for sensitization of lanthanide luminescence specially infrared luminescence of an intensely coloured neodymium and ytterbium mono-thio-β-diketonate chelates. Chauhan[23] synthesized isoxazole derivatives from diaryl-1,3-diketones under microwave irradiation. Hegazy and Al-Motawaa[24] synthesized lanthanide complexes of substituted β-diketones hydrazone derivatives through condensation of β-diketone with aromatic aldehydes followed by reaction with phenylhydrazine.

Korde[25] studied the synthesis & biological screening of metal complexes of 1-(2-Hydroxyphenyl)-3-(4-Ethoxyphenyl)Propane-1,3-Dione. Recently D.M. Suryawanshi[26] studied 1-(2 -hydroxyphenyl)-3-(4-t-butylphenyl)propane-1,3-dione as antioxidant agent. Vaidya S. R.[27] studied the order of stability of complexes of transition metal ions with β-diketone ligands potentiometically. Nabil Bader[28] studied the physici-chemical parameters of the complexes of 2-carboxyphenylhydrazo-acetoacetanilide (2-CPHAAA) with Cu(II), Ni(II) , Mn(II) and Co(II) ions in ethanol-water mixed solvent system. Narendra Bhise [29] studied anti-inflammatory, antioxidant and cyclic voltammetric studies of β-diketone and its metal complexes. Korde[30] studied thermal study of transition metal complexes of β-diketone ligand.

3] Objectives of Research work:

This work focuses on synthesis, characterization and study the biological aspects of metal complexes of β-diketone ligands, five objectives of the work are as follows:

- To prepare various β-diketones and its metal complexes.
- To study the spectral characterization of synthesized compounds.
- To study the solution conductivity and magnetic properties of synthesized complexes.
- To study the antibacterial and antifungal activity of ligand and its metal complexes.
- The result will be used to deal with the structural studies of complexes, nature of bonding and effect of substituents on complexes.

4] Methodology to be adopted:

a) New type of β-diketone can be synthesized by ultrasound irradiation as well as conventional method.

b) Metal complexes can be synthesized by following method:

$$\text{Metal} + \text{Ligand} \xrightarrow[\text{pH maintain}]{\text{Reflux and))))}} \text{Metal complex}$$

All the synthesized complexes characterized by following ways.

1) Physical characterization, analytical and molar conductance.
2) I.R., U.V. and Mass Spectra.
3) Magnetic and electronic absorption spectra.
4) Thermal analysis.
5) Powder X-ray diffraction.
6) Biological aspects.

5] <u>Importance of Study / Society application:</u>

The *β*-diketones can be bonded to metal ions in a variety of ways. The nature of chelation and bonding of these derivatives were first elucidated by Werner and Morgan. *β*-diketones would exist mainly in the enolic form and form metal chelates in the presence of various ions, such as ferric ions(Fe^{3+}),Copper ions(Cu^{2+}) and zinc ions(Zn^{2+}). Recent studies suggest that metal chelates induce apoptotic cell death in various tumour cell lines and are potent antitumour agents for tumour cells including malignant melanomas. Their biological activities as evidenced from their antitumour, antioxidant, antiinflammatory, antiviral and immunomodulatory activities. Thus the properties of *β*-diketones as chelators of metal ions may play an important role in various biological functions of the compound. The present work deals with the studies of metal complexes of β-diketone ligand and its biological importance.

We hope this research work will be useful to scientist, researchers in the different field of applications. It has a nice scope for further development in the future.

It is claimed that result of our research work will be new, basic and original contribution to the research field.

6] <u>Proposed work plan:</u>

Year – wise plan of work and targets to be achieved

<u>I Year plan:</u>

The collection of basic materials required for this research. This includes collection of Journals, Books and some research papers related to the research. We would like to visit few libraries and institutions like TIFR, IICT, NCL, IISER, IITS and some universities for collection of literature. In this year, we will complete course work. Two progress reports will be submitted at the end of this year.

II Year plan:

The collected material will be proceeded and attempt will made to prepare β-diketones and its transition metal complexes. Purification and characterization of β-diketones and its transition metal complexes will be carry out. Also antimicrobial studies of β-diketone ligands and its transition metal complexes will be done. Two progress reports will be submitted at the end of this year.

III Year plan:

The outcome of our research work will be presented in national and international gatherings such as seminars, workshops, conferences during this year. The research work will be published in the several journals. Two progress reports will be submitted at the end of this year and submission of final synopsis will be done in this year.

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